REMARKS

The Office Action dated August 20, 2004 presents the examination of claims 20-21, 23-24, 26-28, 30-31, 34, 37, and 40-43 are pending in the present application. Claims 44-48 are added. Support for the addition of these claims is found in the specification, such as on page 12, lines 9-12, and page 13, lines 10-11. No new matter is inserted into the application.

Interview

An interview was conducted with the Examiner at the United States Patent and Trademark Office on January 11, 2005. Applicants' representative extends gratitude to the Examiner for his assistance in expediting prosecution of the present application.

In the Interview Summary, the Examiner writes,

> Auer et al. reference would fall under Ms. Rupert's argument stating that the artisans, while employing dUTP or dITP, do not involve the use of at least one of 7-Deaza-dGTP or dITP and at least one of 7-Deaza-dATP and hydroxymethyl dUTP. Ms. Rupert was advised that further search would be necessary to determine whether the claims would be free of prior art, however.

The interview was productive, as evidenced by the Examiner's statement that agreement with respect to the claims was reached. When presented with the differences between the prior art and the present invention, the Examiner agreed to withdraw the rejection under 35 U.S.C. § 102 over Auer et al. upon a final review of this

reference. The Examiner indicated that he will conduct another search of the prior art in order to confirm that the claims are novel and non-obvious. Applicants reiterate that many of the prior art references cited by the prior Examiner require the use of dideoxynucleotides, which caused termination of amplification. As recited in the instant claims, the nucleotide analogs of the present invention do not cause termination of the amplification reaction.

Applicants respectfully submit that the remarks presented herein fully address on the record the novelty and non-obviousness of the claims of the present application. The Examiner is therefore respectfully requested to withdraw all objections/rejections of record and issue a Notice of Allowability indicating the patentability of claims 20-21, 23-24, 26-28, 30-31, 34, 37, and 40-48.

Abstract (Page 3 of the Office Action)

The Examiner objects to the abstract for containing more than 150 words. In order to overcome the objection, Applicants submit herewith a new abstract containing less than 150 words. Withdrawal of the instant rejection is therefore respectfully requested.

Claim Objections(Page 3 of the Office Action)

The Examiner objects to claims 42 and 43 for being dependent upon a subsequent claim rather than a proceeding claim. Applicants

respectfully traverse. Reconsideration and withdrawal of the instant objection are respectfully requested. The Examiner is respectfully requested to renumber the claims consecutively in proper order once the claims are deemed allowable in accordance with 37 C.F.R. § 1.126.

Rejection under 35 U.S.C. § 102(b) (Pages 3-4 of the Office Action)

The Examiner rejects claims 20 and 21 under 35 U.S.C. § 102(b) for allegedly being anticipated by Auer et al. (*Nucleic Acid Research*, 24:5021-5025 (1996)). Applicants respectfully traverse. Reconsideration and withdrawal of the instant rejection are respectfully requested.

On page 3 of the Office Action, the Examiner asserts,

> Auer et al. disclose a method selectively amplifying DNA sequences from cDNA, said method comprising the steps: i) generating a first strand cDNA from an RNA via reverse transcription reaction, wherein said reverse transcription reaction employs nucleotide analogs dUTP and dITP; ii) preparing a second strand cDNA from the generated first strand cDNA employing the same nucleotide analogs; and iii) amplifying the double stranded cDNA via use of the same nucleotide analogs to ensure that the duplex formed between the newly generated cDNAs have a melting temperature well below that of the duplex formed between the genomic DNAs….

As discussed during the interview, Applicants respectfully disagree with the Examiner's characterization of the Auer et al. reference. Contrary to the Examiner's remarks, Auer et al. fails to disclose each and every feature of the instant claims.

Specifically, Auer et al. fails to disclose the use of at least two nucleotide analogs. As recited in claim 1, the reverse transcription reaction in the present invention occurs in the presence of at least one nucleotide analog selected from the group consisting of 7-Deaza-dGTP and dITP, and at least one nucleotide analog selected from the group consisting of 7-Deaza-dATP and hydroxymethyl dUTP.

In contrast, Auer et al. teaches RNA selective amplification using dITP as the only nucleotide analog during both the reverse transcription reaction and second strand cDNA synthesis step, as shown in Figure 1. Auer et al. teaches that dITP was used in order to reduce the strand separation temperature of the DNA·DNA duplex or the RNA·DNA hybrid (see, page 5022, lines 1-13 of the right column).

Further, Auer et al. only uses hydroxymethyl dUTP for initial RNA selective amplification experiments (as noted on page 5022, right column, under "Results and Discussion"). Auer et al. never teaches or suggests the use of hydroxymethyl dUTP in combination with another nucleotide analog during amplification.

In addition, dUTP was used for the dUTP/UNG carryover prevention strategy (see, page 5023, lines 33-42 of the right column, and Figure 3). However, Auer et al. never discloses whether or not the use of dUTP results in reduction of the strand separation temperature of the DNA·DNA duplex or the RNA·DNA hybrid.

Furthermore, the incorporation of dUMP during PCR requires pretreatment of the PCR amplification with UNG (uracil N-glycosylase) activity.

In summary, Auer et al. never teaches or suggests preparing a cDNA comprising at least two kinds of nucleotide analogs by a reverse transcription reaction using an RNA as a template in the presence of at least one nucleotide analog selected from the group consisting of 7-Deaza-dGTP and dITP, and at least one nucleotide analog selected from the group consisting of 7-Deaza-dATP and hydroxymethyl dUTP. For this reason, Auer et al. fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner rejects claims 23-24, 26-28, 30, 34, 37, and 40-43 under 35 U.S.C. § 103(a) for allegedly being obvious over Auer et al. in view of Dodge '117 (U.S. Patent 5,912,117, of record) in light of Swanson (*The Scientist*, 13(4):265, February 15, 1999). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

As a preliminary matter, Applicants respectfully point out that Swanson was published on February 15, 1999. However, the priority date of the present application is August 14, 1997 (international filing date: August 10, 1998). Therefore, Swanson is

not a prior art document at the time of filing the present application. Withdrawal of the Examiner's reliance on Swanson is therefore respectfully requested.

Applicants respectfully submit that one of ordinary skill in the art would never have achieved the present invention from the disclosure of Auer et al., either alone or in combination with Dodge '711.

The skilled artisan would not have expected that selective amplification of the DNA of a target sequence derived from RNA can be achieved by the use in combination of a nucleotide analog selected from 7-Deaza-dGTP and dITP and a nucleotide selected from 7-Deaza-dATP and hydroxymethyl dUTP. Even if dITP was hypothetically replaced with hydroxymethyl dUTP in the method of Auer et al., one of ordinary skill in the art would merely achieve an RNA selective amplification method using one of hydroxymethyl dUTP or dUTP. There is simply no suggestion in Auer et al. to carry out a reverse transcription reaction in the presence of at least one nucleotide analog selected from the group consisting of 7-Deaza-dGTP and dITP, and at least one nucleotide analog selected from the group consisting of 7-Deaza-dATP and hydroxymethyl dUTP.

The Examiner relies on Dodge '117 merely to teach a compound for lowering Tm value. The addition of Dodge '117 does not make up for the deficiencies Auer et al. In other words, a combination of Dodge '117 and Auer et al. still fails to disclose or suggest a

reverse transcription reaction in the presence of at least one nucleotide analog selected from the group consisting of 7-Deaza-dGTP and dITP, and at least one nucleotide analog selected from the group consisting of 7-Deaza-dATP and hydroxymethyl dUTP.

Therefore, the cited references fail to render the present invention obvious under 35 U.S.C. § 103(a). Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the outstanding rejections and objections. For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the outstanding rejections and objections, and to issue a Notice of Allowance indicating the patentability of the present claims. Early and favorable action of the merits of the present application is thereby respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to January 20, 2005, in which to file a reply to the Office Action. The required fee of $430.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By _____
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1422-0411P

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Attachment: Abstract